Drug restores brain function and memory in early Alzheimer's disease

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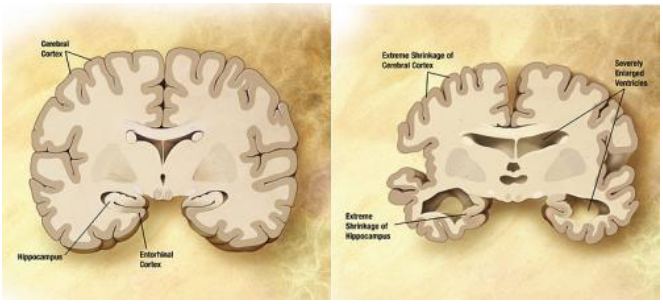

Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

A novel therapeutic approach for an existing drug reverses a condition in elderly patients who are at high risk for dementia due to Alzheimer's disease, researchers at Johns Hopkins University found.

The drug, commonly used to treat epilepsy, calms hyperactivity in the brain of patients with amnestic mild cognitive impairment (aMCI), a clinically recognized condition in which memory impairment is greater than expected for a person's age and which greatly increases risk for Alzheimer's dementia, according to the study published this week in *NeuroImage: Clinical*.

The findings validate the Johns Hopkins team's initial conclusions, published three years ago in the journal *Neuron*. They also closely match the results in animal studies performed by the team and scientists elsewhere. Next, neuroscientist Michela Gallagher, the lead investigator, hopes the therapy will be tested in a large-scale, longer-term clinical trial.

Hippocampal over-activity is well-documented in patients with aMCI and its occurrence predicts further cognitive decline and progression to Alzheimer's dementia, Gallagher said.

"What we've shown is that very low doses of the atypical antiepileptic levetiracetam reduces this over-activity," Gallagher said. "At the same time, it improves memory performance on a task that depends on the hippocampus."

The team studied 84 subjects; 17 of them were normal healthy participants and the rest had the symptoms of pre-dementia memory loss defined as aMCI. Everyone was over 55 years old, with an average age of about 70.

The subjects were given varying doses of the drug and also a placebo in a double-blind randomized trial. Researchers found low doses both improved memory performance and normalized the over-activity detected by functional magnetic resonance imaging that measures brain activity during a memory task. The ideal dosing found in this clinical study matched earlier preclinical studies in animal models.

"What we want to discover now, is whether treatment over a longer time will prevent further cognitive decline and delay or stop progression to Alzheimer's dementia," Gallagher said.

Other team members from Johns Hopkins included Arnold Bakker, assistant professor of psychiatry and behavioral sciences; Marilyn S. Albert, director of the Division of Cognitive Neuroscience in the Department of Neurology; professor of neurology Gregory Krauss and the clinical study coordinator, Caroline L. Speck.

Gallagher, the Krieger-Eisenhower Professor of Psychology and Neuroscience, is the founder of, and a member of the scientific board of, AgeneBio, a biotechnology company focused on developing treatments for diseases that affect brain function. The company is headquartered in Baltimore.

Gallagher owns AgeneBio stock, which is subject to certain restrictions under Johns Hopkins policy.

She is entitled to shares of any royalties received by the university on sales of products related to her inventorship of intellectual property. The terms of these arrangements are managed by the university in accordance with its conflict-of-interest policies.

More information: *NeuroImage: Clinical*, dx.doi.org/10.1016/j.nicl.2015.02.009

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